

Part III

Synthesis

Chapter 8

Synthesis

My specific goal is to revolutionize the future of the species. Mathematics is just another way of predicting the future.

Ralph Abraham

8.1 AN OVERVIEW OF THE CONCLUSIONS

8.1.1 Population dynamics

- An integration of population dynamics models was achieved. The per capita growth rate does not depend on the population size. Still it recovers determinate and indeterminate growth patterns such as: exponential, potential (hyperbolic and parabolic), logistic, θ -logistic, and Gompertzian. It also includes models of ontogenetic growth. It has other regimes consistent with several ecological and evolutionary models (although this needs further work to make a formal statement).
- The carrying capacity is not invoked as a fundamental concept for density dependence. It arises from certain initial conditions and combination of parameters. The conditions not leading to carrying capacity (i.e. models of indeterminate growth) are still biologically plausible. Furthermore, assuming a carrying capacity might limit our understanding of the ecological processes.
- General patterns of scaling laws were found, which concerns not only population dynamics but also ontogenetic growth laws. This broadens our view on the question and usefulness of scaling as a tool.
- There are further ways in which populations can be randomly affected, more than just environmentally or demographically: perturbations affecting the inter-specific interaction parameter θ , depending on the "noise to signal" relation, will result in populations that resemble either (a) logistic growth, or (b) exponential growth. On the one hand, this provides a further explanation for the ubiquity

of these growth laws. On the other hand it compromises mechanistic explanations for these patterns. Mechanistic explanations would have little use, in contrast with an understanding of the sources of the fluctuations. In the logistic cases, the stable size is uncorrelated with the deterministic carrying capacity. This is further evidence that threatens the idea of carrying capacity.

8.1.2 Population Genetics

- The idea of *entropy* was formalized for population genetics. It is a measure that is maximized at equilibrium, and accounts for the expected contribution to the evolutionary potential by selection, mutation and drift.
- Based on the previous, a coupling between population and quantitative genetics was achieved through an analogy with statistical mechanics. The methodology is general, but explicit results were performed for additive traits (including dominance effects) under directional or stabilizing selection, and for multivariate traits with pleiotropic effects, subject to directional selection.

The coupling is not restrictive on the effects and number of the loci, dominance, pleiotropy, or epistasis. It depends however on Hardy Weinberg and linkage equilibrium, diallelic loci, and constant population sizes. It is essentially frequency-independent.

- This method avoids the arbitrary choice of the quantitative variables that are needed to track evolution. It gives a neat way to choose the variables needed to track evolution.
- Knowledge of the allele frequencies is not required to make predictions. Alternatively the predictions are for the ex-

pectancies of the quantitative variables, which only depend on macroscopic quantities.

- It is possible to make long-term predictions of evolution, provided that we know the breeding values, the mutation rates, the size of the population, and the strength of selection. But we do not require to know the allele frequencies at any locus. This is particularly true for the values of the traits in an 'average' population, but also for the genetic variance, the \mathcal{G} -matrix, and any other quantity that depends on the allelic effects.
- Specific results:
 - For directional selection, high mutation rates ($4N\mu > 1$) and drift, the quasi equilibrium dynamics assumption and the statistical mechanical approximation are accurate in predicting the evolutionary course of polygenic traits.
 - The statistical mechanical method has to be modified for very low mutation rates ($4Nm \ll 1$). For intermediate mutation rates ($4Nm \simeq 1$) and directional selection, the inclusion of dominance effects allow a correct coupling between the micro and macro states.
 - The extension to multivariate traits was achieved by including several traits as observables. This allows pleiotropic effects to be included.
 - The change in the \mathcal{G} -matrix can be computed following the statistical mechanics methodology, and it includes the action of selection, and mutations, averaged over drift.
 - \mathcal{G} is much more sensitive to drift effects than to selection. Mutation does not change the direction of evolution, although it affects the rates of change of \mathcal{G} . The

pleiotropic effects over \mathcal{G} 's eigenstructure are more noticeable at high mutation rates; strong pleiotropism has only a minute effect over \mathcal{G} if mutation rates are low.

8.2 FURTHER EVOLUTIONARY IMPLICATIONS

The most pervasive trait of populations –in the broadest sense– is that their sizes dynamically change and adapt to specific ecological conditions. In itself population growth is a cornerstone of the evolutionary theory. It is so conspicuous that the evolutionary mechanisms responsible for fixating a given strategy of growth pass inadvertent, and typically these patterns are often assumed as an intrinsic property of an organism. For example, the concept of Malthusian rate of growth is typically used in several evolutionary theories in order to evaluate whether a mutant will invade a population or not. Typically, this approach goes in hand with the assumption that populations remain in their carrying capacity along the evolutionary process. In this sense, the question of quantity is deferred, focusing on the question of quality, that is whether the mutants perform better than the residents. This is the view from the game theoretical and adaptive dynamics theories. A second field that employs equivalent assumptions is population genetics. The difference can be on the recursive nature of the mutants. But when these mutants are rare, the evolutionary analysis is equivalent to that of adaptive dynamics. Life history theory on the other hand, provides explanations on what determines this Malthusian rate of growth, r_{\max} , interpreted as the maximal rate of increase of a rarified population on ideal ecological conditions (Fisher, 1930; MacArthur and Wilson, 1967; Stearns, 2004; Charnov, 1993). Thus these three theories –adaptive dynamics, population ge-

netics, and life history theory- seems to build a fairly rounded-up picture of evolution.

The mathematical models of population dynamics often employ carrying capacity as a mechanism to regulate populations, modeling the ecological constraints on growth. The canonical model, the logistic equation, predicts that the population will attain equilibrium at the carrying capacity. When growth is determined, “equilibrium” and “carrying capacity” become one and the same. However, the notion of carrying capacity, defined in terms of the equilibrium of a population can often be misleading and ill-defined. With ill-defined I mean that carrying capacity ambiguously takes as equivalent (i) the equilibrium size of the population and (ii) the maximum number of individuals sustained in the environment, determined by ecological factors. This, although a common practical equivalence, can be regarded as non-scientific. Defined as above, we cannot distinguish whether the population reaches equilibrium because the environment is saturated, or the environment has been saturated *because* the population has reached equilibrium. There are obviously numerous examples against my statement, where it is well determined how the ecological constraints determine a population’s carrying capacity (e.g. life history theory approaches the problem in several ways). But the concept, being a cornerstone of population dynamics and genetics, tends to be more phenomenological than mechanistic. I consider that it is possible to study some general properties that determine not only carrying capacity, but also other traits that determine growth.

To start, the Malthusian rate of growth, since the seminal works of Sir Ronald Fisher (1930, Ch. 2), has been conveyed with genetic structure. But other descriptors of growth –like carrying capacity– are not so easily equated into evolutionary and genetic terms. The Malthusian fitness is a very natural

measure of growth, and under fixed population size it links the genetics to a phenotype's rate of growth in simple terms. Other traits involved in growth regulation have to invoke more specific mechanisms in order to be equated to genetic variables in a coherent way. Otherwise, we might work in terms that are very general, but give little evolutionary insight. To follow, since the decomposition of the population growth dynamics into population size and growth rates involves only two parameters in a linear way, it immediately provides a simple set-up to consider evolutionary implications. (Not that a different formulation would not allow it, but the simplicity and generality of the model opens the possibility for simpler evolutionary analyses.)

The question in general terms, is which evolutionary and genetic properties are present in a reproducing system, which determine a growth pattern. The idea can be approached from distinct sides of the evolutionary theory. I will digress in three directions: life-history, invasion analysis (game theoretical approach), and population genetics.

Life history

To begin with, I will give an example on how we can set-up the growth equations in an independent way of the carrying capacity. The first step has already been achieved in the size-rate decomposition, where an explicit dependence on the carrying capacity N_∞ has been achieved¹. We could say that N_∞ , the equilibrium size, is 'hidden' in the initial conditions or the per-capita rate –as I showed in Eq. 1.20, but beware that this equation is not general, since there might not be a carrying ca-

¹Note that I changed the notation with respect to Ch. 1: I will use now N to denote population size, rather than x , in order to give a more intuitive association to the symbol, and which hopefully avoids miss-understandings in the following equations.

capacity at all. But we can take a different route, and relate the initial growth rate to life-history parameters. For instance, at very low population sizes where the density dependence is the weakest, the rate will be maximal (that is a perturbation of r from the fixed point ρ/θ , Eq. 1.9). Instead of equating the initial rate of growth to a carrying capacity as in Eq. (1.20), we can borrow the interpretation from life history, and equate it to r_{max} , which for textbook examples we can take as a function of other life history parameters (e.g. $r_{max} \simeq \log(R_0)/T_c$, where R_0 is the lifetime reproductive success, and T_c the generation time; Charnov (1993) Eq. 6.6, pp.118). Hence, equating the initial rate of growth as $r_{(0)} = r_{max}$, then it follows from Eq. 1.5 that

$$-\alpha = \left(\frac{\theta r_{max}}{\rho} - 1 \right) N_0^{-\theta} = (\theta \log(R_0) - 1) N_0^{-\theta} \quad (8.1)$$

Now, introducing into 1.5, we get:

$$r_{(t)} = \frac{\rho}{\theta} \left[1 + (\theta \log(R_0) - 1) \left(\frac{N}{N_0} \right)^\theta \right] \quad (8.2)$$

Thus mutants with distinct strategies of ρ, θ and R_0 , might exploit the ecological constraints in different ways allowing distinct patterns of growth can be evolutionarily stable, and which may –for example– show different limiting sizes N_∞ . Consider the point N^* at which the maximal change of speed of the per-capita rate is attained, that is $d(Nr)/dN = 0 \rightarrow r^* = \rho/(1 + \theta)$. Introducing this into Eq. 8.2, we get that

$$1 = (1 + \theta) (\theta \log(R_0) - 1) \left(\frac{N^*}{N_0} \right)^\theta \quad (8.3)$$

I assumed that the product ρT_c –the average number that a female would produce in a rarified condition– is of the order of 1. The last expression has some implications. First, if we fix θ ,

then we have a relationship between R_0 and N^* . It is convenient to measure N^* relative to the carrying capacity: $\eta = N/N_\infty$, so that the term $N^*/N_0 = \eta^*/\eta_0$. If we introduce and re-arrange Eq. 8.3, we have that

$$\eta^* = \eta_0 [(1 + \theta)[\theta \log(R_0)]]^{-1/\theta} \quad (8.4)$$

If we map to a semi-log scale, we can express this relationship as

$$\eta^* = A - B \log \log(R_0). \quad (8.5)$$

This relationship is known in life-history theory as *Fowler's rule*, explaining that species that share an R_0 will also share η^* (Fowler, 1988). Fowler identified this relationship in an empirical way, and to my knowledge it has not been related to θ -logistic models in the way I have presented. This is relevant, because Sibly et al. (2005) analyzed a substantial data set of population dynamics in order to measure the distribution of the intra-specific competition coefficients, and have shown that the parameter is distributed over a large range (± 100) for distinct taxa: mammals, birds, fish, and insects. The distribution is different across taxa, and remains to be explained. Yet it suggests that Fowler's rule is a coarse-graining of a more detailed version as the one I have presented. Thus, if we plot different curves with different values of θ in the range reported by Sibly et al. (2005), and superimpose Fowler's data (listed in Charnov, 1993, pp.), we can see that considering additional information, that is the value of θ , can give more precise explanations of the data (Fig. 8.1 A). In other words, the competition parameter can explain the deviations from the main trend.

Second, if we fix the point of inflection N^* , then there is an inverse relationship between the degree of competition and the life-time reproductive success. If R_0 is increased, then θ is diminished (intra-specific competition decreases). As a by-product then, the amount of individuals that are maintained

in the population is also increased (the limiting size is bigger). If on the contrary, competition is high, the life time reproductive success decreases, and there is, in equilibrium a smaller population size. But, is there any invariant involved in this relationship? Indeed, some algebra leads to the relationship

$$\log \log(R_0) = A_2 - \log(\theta) . \quad (8.6)$$

Formally A is between 0 and $\log(2)$. The choice $A = 0$ gives a perfect fit for big values of θ (as the trend shown in Fig 8.1 B), whilst the choice $A = \log(2)$ fits better the lower values. In any case, the deviations are not big in the log-log scales, and an unbiased survey of data would give probably $A \sim \log(2)/2 = 0.35$. I am enthusiastic and eager to go forward to check my predictions!

Game-theoretical approach

The common approach to density dependence is that it is determined by the ecological conditions. Because the environment would itself be able to support only a maximal amount of individuals, then a carrying capacity would be established. This could well be in many (or even most) situations. But I would like to speculate in a different direction. If a population that does not have a density dependence mechanism that leads to a limit size “consistent” with ecological constraints, then this population would eventually go extinct. This can be most easily pictured with an island model as a proxy (MacArthur and Wilson, 1967), allowing study the evolution of growth rates. For example if mutant individuals that are able to adapt their growth response to the ecology in a coordinated and coherent way invade a resident population, then these new variants would (by definition) be better adapted, and their extinction would be less

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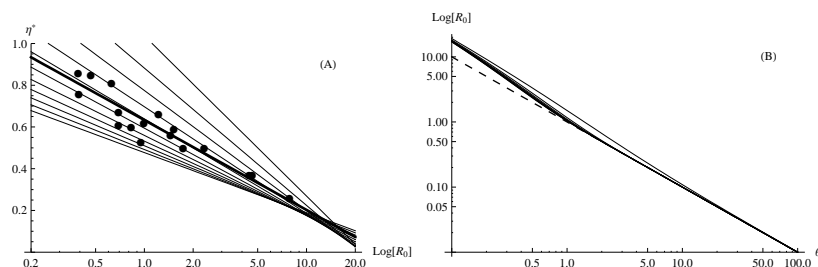


Figure 8.1: Life-history invariants related to growth parameters. (A) Fowler’s rule points an inverse relationship (in semi-log scale) between life-time reproductive success, and the point at maximal growth rate. His fit (dark line) to the data (black dots) is given by Eq. 8.5 with $A_1 = 0.633$ and $B = 0.187$. The thin lines show the same relationship but with A_1 computed explicitly with distinct values of θ in the range (3, 8) (spaced every 0.5 units). (B) A predicted invariant between the intra-specific competition parameter θ and life-time reproductive success, in log-log scale. The invariant relationship is surprisingly simple, and independent of any other parameter. The dark dashed line is a simple approximation (Eq. 8.6), whereas the thin lines are the exact values employing a range of inflections N^*/N_0 in the range (1, 16). In this case $A_2 = 0$ (see text for explanations).

likely. Also, they would out-compete any new invader, and dispersing to other island, they would be established.

Thus, to evaluate if the mutant will invade, we can compare their Malthusian rates (Maynard-Smith, 1999). If for example the density dependence affects the mutant equally as any other resident, then the invasion analysis reduces to compare the ratios

$$\frac{\rho_M}{\theta_M} > \frac{\rho_R}{\theta_R} \quad (8.7)$$

where M refers to the mutant strategy, and R to the resident strategy.

An interesting feature, is that if a mutant appears that has θ close to zero (a mutant that is not strongly competitive, or cooperative, with its mates), then it will most likely invade. That

mutant, will of course have a Gompertzian growth rate (because $\theta = 0$ corresponds to this strategy, see Ch. 1). If that is the case, the question is why Gompertzian growth is not conspicuous in populations? Basically, I am just saying that the mutant can invade, which does not mean it can actually replace the resident. That would depend on how the mutants and residents interact. But also, there might be constraints that keeps θ fixed, like strong selection to maintain some degree of competition (e.g. sexual selection, or limited resources).

Gompertzian growth implies that there is no intra-specific competition, yet there is density regulation. At this stage, it matters little what the Malthusian rate of growth is: a Gompertzian growth will outcompete any other determinate population growth strategy. What happens once a Gompertzian strategy has invaded? Naturally then, evolution will favor larger Malthusian parameters. I am of course assuming that there are no trade-offs between ρ and θ . It is not difficult to develop in such direction, but under linear trade-offs it is easy to see that still a Gompertzian strategy will invade, and the Malthusian rate would be maximized.

The analyses of Sibly et al. (2005) have shown that the competition parameter θ has a broad distribution. Although there is a substantial proportion of strategies with $\theta \simeq 0$, other values are frequent. Thus my analysis is clearly missing something. First of all, I have computed only the probability of invasion, and not really analyzed whether the mutant will fix, and reach an evolutionarily stable strategy. Also I have ignored other ecological factors. As simple analysis shows that inclusion of other factors will not lead to distinct results. For example, in an island model, where there is certain probability P_x of becoming extinct, then the fitness has to be weighted by these chances.

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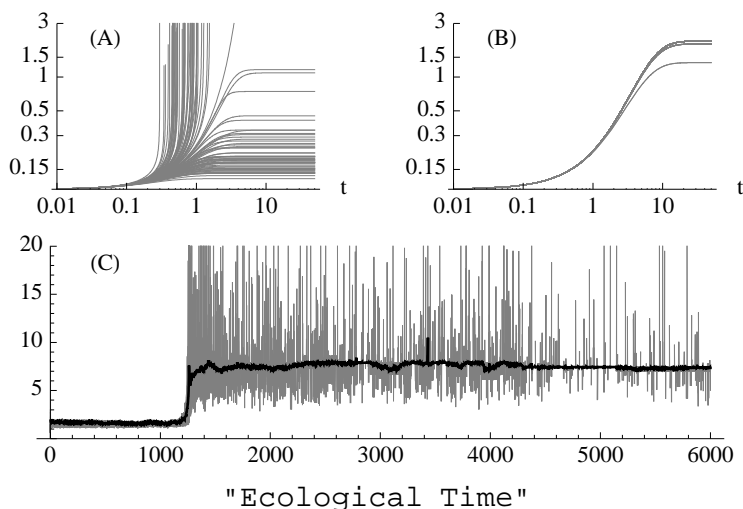


Figure 8.2: Evolution of population patterns. 100 random populations strategies, (ρ, θ) were allowed to evolve for 6000 ecological episodes (events of extinction, re-colonization, or invasion). (A) Dynamics of the initial founder populations. (B) Dynamics of the evolved strategies (after 6000 ecological episodes). In both cases, time is in generations. (C) Sizes of each population once they have reached equilibrium after an episode -i.e. "carrying capacities" of each population- (gray lines), and the average size of the whole pool of populations (black line), time is measured in ecological episodes.

In short, the invasibility is determined by

$$(1 - Px_M)r_{MR} \geq (1 - Px_R)r_{RR} \quad (8.8)$$

The chances of survival $(1 - Px)$ are related to the size of the population, life-time reproductive success, etc. An thus we can expect that consideration of a more structured model accounting for these factors, can give predictions on how the patterns of growth can be fine tuned. In Fig. 8.2 I performed a simple simulation, where a population has a given chance of becoming

extinct if it is below a certain size, or above a limiting environmental sustainable capacity. The populations are able to evolve their strategies every generation, and if the mutant is able to invade, then it replaces the resident. The value of r_{\max} is fixed, but together with the strategy (ρ, θ) determines the value of N_{∞} . The survival is decided only after populations have achieved equilibrium. Some combinations of these parameters will lead automatically to extinctions or to explosion, as explained in Ch. 2. In both cases extinction is certain. The results show that (a) the populations do not typically evolve to have a carrying capacity that matches the maximal ecological sustainable density, but rather reach a state of mutation-selection balance, and (b) the populations tend to diminish their intra-specific parameters quite close to zero.

A substantial deal of work is required to gain a clear understanding of the evolution of patterns of growth. Most critically, the way how the mutant and the resident interact will most surely change the Gompertzian outcome.

Genetics

Regarding a growth strategy as a quantitative character can be a complicated matter. Naturally, the distribution of the characters are determined by the frequency of the alleles. But since the evolution of a structured population is driven by its phenotypic distribution, its change feeds back into the distribution of allele frequencies. Ignoring mutation, linkage and drift, Slatkin (1980) studied the effect of population competition on the displacement of a quantitative character. The replication rates (fitness) depended directly on the fitness of the character. In this model the genetic variables were not tracked, but instead it was assumed that both the trait and the genetic variance were changing in time, and thus determining the broadness

and position of the distribution of the trait. Doebeli (1996b) extended the model to include the genetic variables, showing that the distribution of genetic effects will be neither Gaussian, nor in demographic equilibrium. This of course raises the question on how robust is the assumption in population genetics (taken along this thesis) that populations are at a demographic equilibrium. But perhaps most important is the question on how sensitive are the conclusions of population genetics with respect to the demographic equilibrium assumption.

It is possible to extend the Wright-Fisher model studied before to the case where population size is changing. For instance, calling n the number of favorable alleles, then the frequency is given by $p = n/2N$. If we compute the rate of change then we obtain

$$\dot{p} = p \left(\frac{W}{\bar{W}} - 1 \right) - pr \quad (8.9)$$

where r is the per-capita growth rate of the population, as above. Thus a quantitative trait that does not affect the growth rate directly will still have some transmission bias due to the effects of population growth. At demographic equilibrium the growth rate vanishes ($r = 0$), and the dynamics would proceed normally through a Wright-Fisher model. If population size changes slowly, then obviously there will be no big deviations from the condition of demographic equilibrium, because the genetic variables mix quickly. However, the situation is typically the contrary: populations tend to change faster than the rate at which mutants appear.

If the dynamics of the population are stochastic, then we can study the joint distribution of allele frequencies and population size. This is not so far from the previous situation, so no particular deviation is expected. In principle, we can easily propose a quasi-equilibrium model, where the local variables $N\mu^*$ and $N\beta^*$ follow a continuous change in N . This should work fine

unless $N\mu^*$ falls below $1/4$. As we saw in Ch. 3, fluctuating selection intensities will still give allow a good approximation from the statistical mechanics methodology. Thus from that side, there is a wide margin for confidence on the demographic equilibrium assumption.

Most interesting is the case where the traits involved in growth (Malthusian and intra-specific competition parameters, as well as “carrying capacity” or any other associated life-history trait) are affected by many genes. As Slatkin (1980); Doebeli (1996b) did, we can define the growth rate of the population as the mean fitness, and then confer it with genetic structure. Equation 8.9 is suggestive of this situation, since from the gene’s point of view, selection and growth rates are two kinds of the same. Defining growth rates directly as mean fitness will determine certain patterns of growth, but it will not provide self-regulation. There is still an effect of population size, because it plays a role in the transmission of alleles to the next generation. Nevertheless, the demographic path will depend *only* on the nature of the selective process triggering evolution.

But to conclude the analysis of the evolution of population dynamics, we can consider the genetic effects over the parameters of growth. In that case the rate equation (1.7b) has some extra terms, because its rate of change would be influenced by the rate of change of ρ and θ . In that case, it is not easy even to separate the time scales, because there are two factors affecting r ’s rate of change. First the density dependent component, which has been studied in the first part of this thesis, and in the above sections of this synthesis. Second, the quantitative rates of change. As indicated by Eq. 8.9 there is a directional effect. This mutual feedback is the source of many complications. So questions about variability maintained by a density dependence term, are not trivial to deal with, but have an interesting richness of properties (see Bürger and Gimelfarb,

2004, for an example of stabilizing selection over a quantitative character mediating competition, and even leading to speciation; Nagylaki, 1979).

For a moment, we can forget about selection, and consider only mutation and drift. This not quite a neutral process, because there is the selective effect of the population dynamics:

$$\frac{d\bar{z}}{dt} = -(2\mu + r)\bar{z} + \text{"drift"} .$$

Where "drift" is Gaussian and has variance proportional to $1/2N$. If the dynamics of the population size is slow (e.g. close to an equilibrium), and the mutation rate high enough ($\mu \gg r/2$), then the rate of change of the trait would be a stochastic process with a stationary Gaussian distribution²:

$$\bar{z} \sim \frac{\sqrt{\mu/\pi}}{2N} \exp[-\mu\bar{z}^2/2N].$$

If the trait in question is the parameter θ , then these fluctuations would be of the kind studied in Ch. 2. Then genetic effects over the intra-specific competition parameter are a parsimonious explanation for this kind of stochastic effects leading to density regulation. Of course, if the character is entirely neutral, then there is no mechanism to control population equilibrium size. We would expect, on the other hand, that if selection for this parameter exists, then the mechanism of density dependence would be genetically determined, and given the noise-suppression nature of the dynamics, and would not require a fine tuning. Unfortunately, the regime $\mu \gg r/2$ is not a biological paradigm. Rather the contrary is expected to happen. There is a situation, however, where we expect to find a high mutation rate, which I analyze in the following section, and that is on the evolution of prebiotic replicators.

²This would be essentially what is called an *Ornstein-Uhlenbeck process*.

Replicators: density dependence in the origins

In the early stages of life's origin, the proto-organisms would lead the prebiotic world in a democratic way. Virtually any possible mutant that appeared would survive (Szathmary and Gladkih, 1989). These prebiotic entities, essentially replicating RNA molecules, would need of each other to replicate, but in a way that any variant molecule would be able to catalyze the replication of any other molecule. Eigen (1971) has argued that these replicators could not have grown exponentially, because the diversity required for maintaining the evolution of a primitive population of replicators, would simply collapse. This led to the ideas of hypercycles Eigen (1971) and the stochastic-corrector (Szathmary and Demeter, 1987b), which provide solutions to the information collapse problem, but themselves are liable to other problems of invasion of selfish mutants.

Nevertheless, although these ideas are alive and explain the transition from replicators to protocells (Maynard-Smith and Szathmáry, 1997, Ch. 4), a solution to the replicator information collapse came from a simpler idea. Based on experimental models –or ‘artificial replicators’–, (von Kiedrowski, 1986; Scheuring and Szathmary, 2001) found that the rate of growth of the RNA population would be parabolic. Under this assumption of parabolic growth, Szathmary and Gladkih (1989) showed that diversity of RNA molecules would be attained and sustained.

However, although suitable for experimental essays, the system is assumed to be in demographic equilibrium (Eigen, 1971). That is that the total size of the population is constant. It is unlikely, however that there were mechanisms of density dependence in such a primitive world. This assumption of constant population size relies on the fact that the building blocks were a limiting factor. There are reasons to think that this could

have been if the rate of abiotic production of building blocks, i.e. nucleotides, would be slow. But the contrary situation is also plausible, that the building blocks were not a limiting step, specially if the population sizes were rather small and the environment was rich.

Irrespective on the competition details of the replicator system (it might well apply with changing population sizes), indeterminate growth would not be viable. Parabolic growth is indeterminate. Given that reaction catalysis times (on the order from seconds to days) are much faster than evolutionary time, then an explosion of the population size would have occurred practically instantaneous. This sound unlikely, since we would have to explain the transitions to compartmentalization and emergence of mechanisms of density regulation within such a short period. The rate of abiotic production of nucleotides would have been to slow as to allow evolution for very quick reactions if parabolic replicator were to grow to high densities. Here there are two possibilities. Either the dynamic would be driven by the decay and sequestering of the components of unreplicated decaying molecules (Scheuring and Szathmari, 2001), or a mechanism to regulate the growth rate had to be present (or of course both). The former case has been analyzed under the typical population-genetical assumption that the size of the evolving population is constant. Now, I try to give some insights on how this constant size could have been achieved. I argue that the effect studied in Ch. 2, that noise in the parameter θ would stabilize the size of the populations, could have played a role. The question of course is what is the source of this noise. My argument is simple. Although we can assume that in average the order of the replication reaction is $1/2$, we can also think that this value is determined by intermediate states of the replication reaction. Thus distinct RNA mutants might have different values of θ , which depends in a

complicated way on the specific sequence. Thus treating this parameter as a quantitative character, then the expected genetic variance would be, following Eq. D.46, $\langle \nu_\theta \rangle = 2\theta\mu/\beta$. As shown in Ch. 5, if fixation of alleles is unlikely, then the character would be normally distributed. Therefore, the strength of the population-genetical fluctuations over the growth rate (the genetic variance of θ) would allow a moderate rate of growth and even an equilibrium if the rate of decay of the molecules would show significant fluctuations.

Now, if two parabolic replicators are competing, the new mutant is able to invade only if $\theta_M < \theta_R$. The later course (whether there is coexistence or displacement of the resident) depends on further details on the density dependence (Mylius and Diekmann, 1995; Metz et al., 2008). Nevertheless, in general terms, selection would favor lower values of θ . A parabolic replicator of exponent $\alpha < 1$ has a per-capita growth rate with exponent $\theta = \alpha - 1$ (Ch. 1), so in general $\theta < 0$.

For parabolic replicators we would need a genetic variance of less than one. In this way, the exponent would be kept between 0 and 1 in average. Otherwise the replicators would cease to be parabolic and we would incur in the domain of the error threshold.

For example, if we were to assume that (1) there are n_e nucleotides which actually affect the value of θ , (2) the mutation rates were relatively high, say $\mu \sim 10^{-3}$, (3) that selection is weak $|\beta| \sim 10^{-2}$, and (4) that $\theta \sim 1/2$ then the genetic variance would be on the order of 10^{-1} . This means that $\epsilon_0 = 50$ (in Eq. 2.2). The rates of decay of the RNA molecules are assumed to be low, but with enough fluctuations (assumed to be environmental), then stabilizing the size of the population would require a variance in the decay rate of the molecules on the order of 10^2 , which is too big. On the other hand, if mutation is higher, and or selection lower, the genetic variance can be increased to at about 0.4, which would require a variance on the decay rate of the molecules of about 0.1, even for low decay rates. This is consistent with the co-existence of multiple replicators.

If the genetic variance of θ were too low, for example because selection is strong, then the replicators would not be in a demographic equilibrium. Still, the population as a whole would grow exponentially, rather than exploding in short time.



8.3 RESEARCH PERSPECTIVES

The mechanisms that drive evolution in the wild –natural and sexual selection as well as mutation and drift– are of the same nature at the micro and macro-evolutionary scales. Nevertheless, population and quantitative genetics aim to understand and predict the diversification of populations into two lineages, that is speciation. One of the problems, which I have addressed since the beginning of my dissertation, is that of variability. The state of the art in understanding genetic variability is to some degree, embarrassing. Theoretical models predict much less variability of what is observed in the wild, and the predictions of the evolutionary course are limited to a few generations. Yet we are attached to our current frame of mind, where we continue to use the very same tools that keep failing. If we compare how difficult is to detect selection at a locus with how easy is to measure molecular substitution rates we find that The Neutral Theory of Molecular Evolution (Kimura, 1985) has provided much more pragmatic use than evolutionary and quantitative genetics, even when we are certain that natural selection is the main cause of diversification in the tree of life. This is exciting, because it reveals that even when our current knowledge accounts for micro-evolutionary processes in an accurate way for artificial selection and experimental evolution, the “natural versions” of evolution seem to be hiding something to us. This is not a trivial subject. There are many lenses between the stars that we want to observe, and the light that gets to our eyes.

The amount of assumptions that we make in order to describe an evolutionary response, or to detect natural selection is not negligible.

1. First of all, we typically assume that populations and species are at evolutionary and demographic equilibrium. This translates into a huge bias in what we are able to mea-

sure. We saw in the second part of this thesis that during transient evolution, we might describe the evolving distribution by local parameters. This means that if at a given moment of time we sample a population and intend to characterize evolutionary factors (mutation rates, effective population size, selective gradients, and even breeding values) then we might have a very wrong picture. For example, we might find dominance effects that are not really there, or miss-estimate the size of a population from genetic markers.

2. Density and frequency dependent effects, as discussed above, not only may have selective consequences that have not been considered in typical quantitative genetical empirical studies, but also coupling selection to population dynamics has major impact on the quantitative measures, affecting the rate of change of quantitative characters.
3. The breeding system, which I have not addressed in this thesis, and sexual selection will entirely change the picture of what we are measuring in quantitative genetics.
4. We are assuming that the genetic effects are constant. The theory of reaction norms have provided clear cut evidence that the distribution of phenotypes change with the environment. There is of course possibility to include genotype-environment interactions that could account for the reaction norms. Nevertheless, whether these interactions are the source of the phenotypic changes across environments has not, to my knowledge been shown. There might be an analogous effect as with the genetic co-variances: because there are statistical associations in the evolutionary response to selection it does not imply that there is at all a genetic association. Interestingly, because the

way how we can identify the pleiotropic QTL's is employing correlated responses, if the genetic effects are not constant across environments the genetic associations could be a by-product of the covariant effects.

This essentially translates in that the effects in the wild environments might actually respond in a totally different way than in the lab, or under controlled experimental conditions. Thus there is little that we can say for the long-term evolutionary response out from association analysis derived from captive populations, experimentally derived estimations (populations that are back-crossed, randomly mated, developed under controlled conditions, etc.) QTL's are part of the optimism for modern quantitative and population genetics, since they give a concrete meaning to the reification of the concepts of locus and allele. Not that these are mistaken, but by their phenomenological nature, they are certainly limited, and often need to be narrowed down (in the best of the cases) to single nucleotide substitutions, in order to have a mechanistic understanding of their effects.

Simple mendelian traits behave very well, and there the concepts of loci and allele work very well. Also the nucleotides in molecular genetics fit very well these ideas. Still, *polygenes* is a very abstract entity. Sometimes their segregation will be reducible to several Mendelian loci, but sometimes not. The number of loci might be very variable, and the number of alleles might as well not be a fixed trait. If their effect is infinitesimal, we are in a safe place, since we can model the effects in a simple and convenient way. Yet in that case the predictions don't go beyond micro-evolution. If the effects, on the other hand are not infinitesimal, the population's course will be sensitive

to the number of alleles and loci. This is rarely taken into consideration.

The effects of modifier loci, although they provide a good theoretical aid, are seldom used empirically to predict and forecast consequences on long term evolution.

In general, most components of the genetic architecture tend to be neglected at the time of quantitative estimations. Although these architectonic elements are invoked often in the practice, they are mostly viewed from the molecular perspective and in a neutral context.

5. There is an underestimation on the meaning of selection differentials. A clear understanding of its meaning is not only essential, but also necessary. A selection differential, relies essentially in another statistical association: the correlation between fitness and the trait. For example, so much work is done on the \mathcal{G} -matrix, trying to understand its response to selection, mutation, drift, migration, etc. But not only the knowledge of \mathcal{G} is of limited interpretation (Pigliucci, 2006), but also in the absence of a concrete measure of selective gradient, \mathcal{G} would say little. From the empirical side, the gradient of selective values is never computed independently of \mathcal{G} (or H^2 , for these matters). In theoretical terms, except in controlled experiments of truncation selection, it is unlikely that we know anything except the local gradient. The result, is that we can only make qualitative predictions. But if we are to be happy with qualitative predictions, then it would make little sense to invest big efforts in accurately determining the genetic structure of a population, if we intend to infer anything about evolution.
6. The last two arguments point to something. If the genetic

effects were constant and the reaction norms would entirely be explained by the genotype-environment interaction, and the micro-evolutionary mechanisms would suffice to explain in the long run macro-evolution, then we would expect to find certain degree of correlation in speciation rates in the bio-geographical gradient. Perhaps this correlation exists, but it is hard at the moments to predict at which (taxonomic) level they should be observed. There are conspicuous cases, like the glaciation periods, where major ecological changes have taken place. But smaller ecological episodes should have not only a notable effect over speciation processes, but also promote it in several lineages.

I would expect this to be so in the case of fixed genetic effects in part because of the universality of the genomic content, in the sense that there are so many genes common (even at distant phylogenetic distances), that at least in traits which are conformed by common genes (e.g. FOX1) there should be correlated responses, at least in particular geographic locations. Honestly I doubt that this would be so. But only because I doubt that these micro-evolutionary mechanisms can be extrapolated to long term under the assumption of fixed genetic values.

Nevertheless, with the local equilibrium approach, we have been able to predict the long term evolutionary response of the genetic co-variances. But these are relying on a constant architecture, a constant population size, and that we know where selection is pointing to. Even with the limitations, this in any case is an improvement, and a constructive methodology, and for which of course I stand. Yet, pointing the failures above is at most useful as a progressive method to see where the limitations are.

These limitations are at best conditions for artificial selection. But if we are to ground the mechanisms of the evolutionary theory only on micro-evolutionary insights, then we might be leaving the back-door open for intelligent absurdities of design, which is a door that we need to close for good.



Bibliography

